California Cancer Commission Studies*

Chapter I

The Cancer Problem

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IN approaching the problem of cancer we are faced with the fact that although our knowledge concerning the disease is continually increasing, there occurs each year a progressively larger number of cancer deaths than ever before. Since 1900 the cancer death rate in the United States has doubled (68.3 per thousand in 1900 to 120.6 in 1935). Official figures from the Bureau of Vital Statistics bring into bold relief this steadily mounting increase in cancer deaths—year after year. As an example, for the past ten years cancer's toll has increased more than 25 per cent.

Year	Cancer Deaths	Year	Cancer Deaths
1936	 142,612	1941	 159,926
1937	 144,774	1942	 163,400
1938	 149,214	1943	 166,848
1939	 153,846	1944	 171,171
1940	 158,335	1945	 177,464
		1946	.... 181,000*

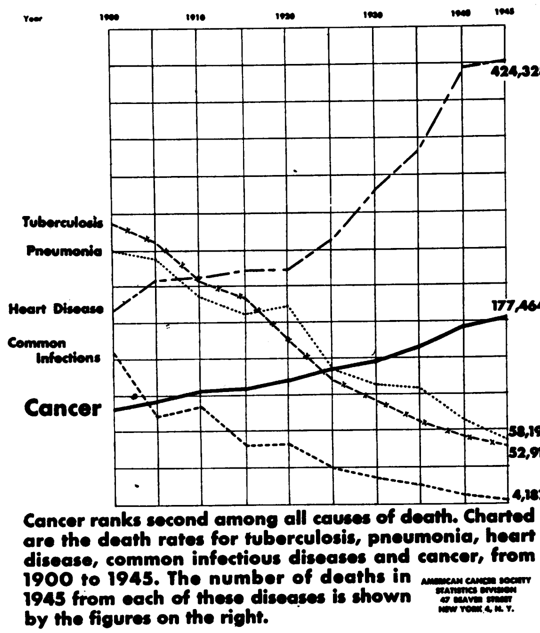
* Estimated by American Cancer Society. All other totals are official figures from the Bureau of Vital Statistics.

In 1946 one out of every eight deaths was due to cancer, indicating that unless our present knowledge is used to full advantage and unless new knowledge is obtained through research 17,000,000 people now living in the United States will die of cancer.

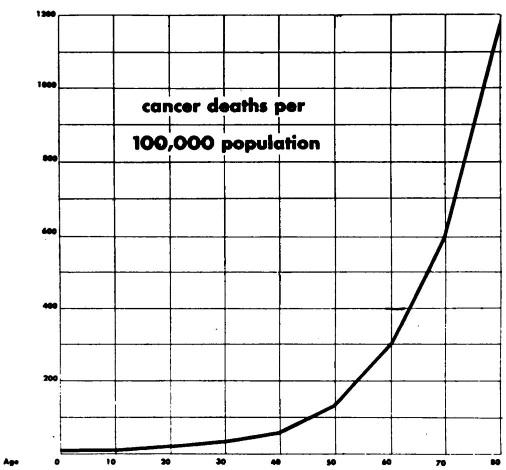
Cancer now ranks second as the most important cause of death. As a killer, it is exceeded only by diseases of the heart.

Is cancer increasing? In spite of the statistics given, the answer to this question is most probably "no." There are two reasons for this answer in the negative. First, the diagnosis and recording of cancer as well as other diseases are becoming ever more accurate, so that cases formerly considered as other diseases are now accurately diagnosed. Secondly, the progressive aging of our population accounts for a major proportion of the numerical increase in the actual number of cancer cases. We have more older people, of cancer age, in our population than ever before in our history. Whereas cancer kills at all age levels, the rate rises sharply after the age of 40. It is estimated that 90 per cent of cancer cases occur after the age of 35.

The degree to which our population has aged in the past 45 years is shown in the Graph 3.



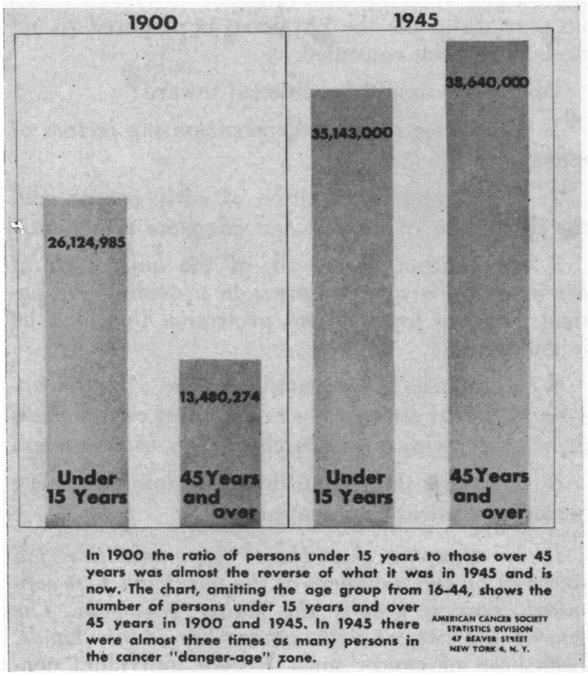
Graph 1.—Cancer, second among the principle causes of death.



Graph 2.—Age, a factor in cancer. Although cancer occurs at all ages the rate rises sharply after forty. Approximately 95 per cent of cancer occurs after 35.

* Organized by the Editorial Committee of the California Cancer Commission.

Approximately 70 per cent of the increase in the published death rate for cancer since 1900 is explained by aging of the population.

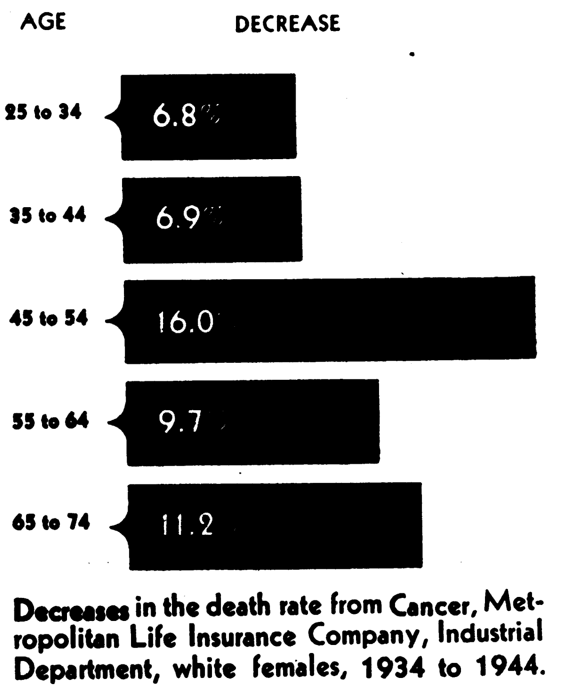


Graph 3.—An aging population. The number of people over 45 has increased markedly and is greater than ever before in our history.

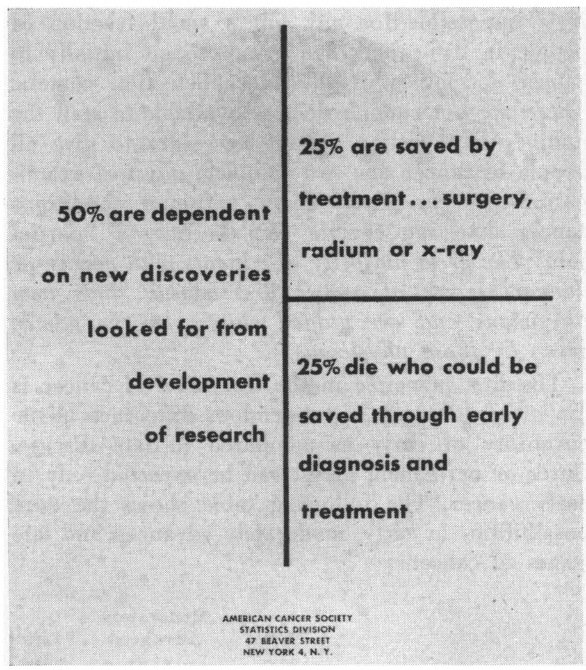
A few encouraging signs in the cancer control program are indicated by statistical studies of selected groups of our population. Such studies pertain to groups or individuals who have been subjected to lay cancer education and who have had access to prompt and adequate treatment. Encouraging trends are noted which indicate, possibly, that with intelligent action on the part of all the peak of the mortality can be passed. For example, in white female policyholders of the Metropolitan Life Insurance Company, for the decade 1934-44, a definite decrease in mortality from cancer ensued for each decade of life. Decreases varied from 6.8 to 16.0 per cent.

The problem of turning the tide in cancer mortality has a number of aspects and presents a definite challenge to the medical profession. At present one out of every four patients with cancer is being cured by present methods (surgery, x-ray, radium), one out of four is dying needlessly due to delayed and inadequate therapy, and two out of four are doomed to die of cancer unless new knowledge and methods are obtained through research.

These considerations bring into sharp focus the *three main fronts on which the attack on cancer must continue—research, education,* and *service.* Of these, the most important is *research* because it is only through a research program that new knowledge and facts can come, facts which will save the 50 per cent of cancer sufferers who are now doomed irrespective of how soon medical aid is sought and the type of therapy instituted. The importance and urgency of the problem deserves preferably coordination on a nationwide scale, with the use of all available trained personnel and facilities. Of



Graph 4.—A decrease in cancer mortality for all decades of life varied from 6.8 to 16 per cent in white female policyholders of the Metropolitan Life Insurance Company from 1934 to 1944.



Graph 5.—One-fourth of the people stricken with cancer are being saved by treatment, one-fourth are dying because diagnosis and adequate treatment are delayed, and one-half are doomed unless new discoveries are forthcoming through research.

practical importance is *education*, not only of the laity but also of the profession, concerning knowledge now available. Education will enable the utilization of tools already in our hands by which we can save one out of every three patients who now needlessly die of cancer. The *service program* with its many ramifications will not only indirectly assist the educational project but will be of great assistance to early and presumably curable needy cancer cases, as well as to incurable patients and their families. This paper will be devoted chiefly to the educational and research considerations of the cancer problem.

EDUCATION OF THE MEDICAL PROFESSION

Education of the medical profession regarding cancer must keep pace with and be closely coordinated with lay education. During the period when many of our doctors were trained, cancer was considered, by and large, as a hopeless problem. Even now, more adequate cancer instruction in many of our medical schools is an imperative need. To mitigate this attitude of hopelessness, care should be taken to show cured and arrested cases of cancer to medical students and members of resident staffs. Cancer postgraduate ("refresher") courses, special one- or two-day clinics for doctors in outlying communities, and lectures for general practitioners are most urgently needed.

It is imperative that the family physician be kept up to date with newer developments in cancer research and that the confidence of the family physician be sought and obtained in any proposed program of cancer control. The family physician is the most important link in our chain of cancer control. Success or failure rests with him. Obviously it is impossible for any but a small fraction of people in the cancer age group to go initially to cancer specialists or to cancer detection centers. There are not enough doctors available to staff the number of detection centers necessary to give all people of cancer age two complete *physical* examinations a year. Even under optimum conditions cancer detection centers can do only a "partial job." *The great majority of patients with cancer or danger signals of cancer first consult their own physicians and are guided chiefly by the advice given by those physicians.*

The first principle in the treatment of cancer is the recognition of the tremendous difference in the curability of early as compared to late disease. Cures or permanent arrest can be expected only in early cancer. The following table shows the cure possibilities in early, moderately advanced and late stages of cancer:

	Early	Moderately Advanced	Late
Skin	95%	25%	?
Lip	95%	25%	?
Breast	75%	25%	?
Uterus—Body	75%	25%	?
Cervix	75%	15%	?

PHYSICIAN MUST BE PREPARED

Educational drives, such as that of the American Cancer Society, are awakening public consciousness, and much accurate information concerning the disease is being disseminated. This will be to no purpose unless the physician is prepared to act decisively when consulted.

His efforts should be directed toward:

1. The recognition of the *predisposing factors of malignancy.*

2. The prompt recognition of *early cancer,* and the institution of *prompt and adequate treatment.*

3. Recognition, above all, of the *limitations of his own ability and resources* in providing the patient with the services and protection to which he is entitled.

4. Willingness to promulgate the *"group approach"* in the study and evaluation of cancer cases prior to evolving prematurely a plan of treatment.

5. Assuming the responsibility of doing complete periodic physical examinations.

It is apparent that these responsibilities fall squarely on the shoulders of the physician first consulted. This is usually the family physician. The fate of the patient with cancer lies in his hands. Each case of cancer must receive individual consideration. Special regard must be given to the natural history (habits) of the particular type of tumor in question. Those specialists likely to be called ultimately to participate in the treatment should be given the opportunity to study each case before a plan of treatment is decided upon, rather than after difficulties have been encountered in attempting to pursue a hastily chosen course. In treating cancer one must have not only the mental but the physical preparation to do the right thing. Of what avail is it to biopsy a bone tumor if facilities are lacking not only for immediate frozen section diagnosis, but for amputation of the part, if necessary?

COMPLETE PERIODIC EXAMINATIONS

Coming more clearly into focus in programs of cancer control is the necessity for complete periodic physical examinations of all well people of cancer age, that is for those over 40 (and preferably 35) years of age. Properly, this job should be done by the family doctor. No physician should refuse to make such an examination at a mutually convenient time. If undertaken, it should not be cursory but should be conducted in a complete, thorough manner, well calculated to accomplish its purpose. In examining patients, regardless of age, the possibility of cancer should always be kept in mind. Inasmuch as such periodic physical examinations are for the purpose of detecting cancer in its early stages, the examination should meet the same minimum standards as those which have been established for "cancer detection centers." Such examinations should include at least the following procedures:

A. History.

B. Routine blood count, urinalysis and serology.

C. X-ray film of the chest (mass survey).

D. *Nose and throat examination,* including lips and intraoral.

E. Examination of the *breasts.*

F. Physical examination of the *chest, abdomen,* and *extremities* (including *skin*).

G. Examination of *lymph nodes:* neck, axillae and groin.

H. *Pelvic examination.*

I. *Rectal examination.*

In order to encourage complete periodic physical examinations in doctors' offices, the Cancer Commission of the California Medical Association is willing to provide, without cost, appropriate examination forms to practicing doctors in California and to provide these forms in sizes to suit the individual doctor's filing systems. (See Figure 1.)

Many early and curable cancers as well as other conditions have been found by careful and complete periodic physical examinations. When abnormalities are found on examination they must be studied until the question of malignancy is settled. The motto should be "look and see," never "wait and see!" Hemorrhoids may well be associated with early cancer. To the chagrin of the medical profession an average interval of nine and one-half months elapses between the time a patient with rectal cancer develops symptoms and the time he obtains definitive treatment. The last four and a half months of this interval is spent with doctors who "wait and see!"

The most worthwhile service the general practitioner can render his patients who have cancer is prompt initiation of the processes through which they will obtain the best diagnostic and therapeutic services possible. The many advantages of the *"group approach"* to cancer are lost if judgment as to treatment plan is passed before all pertinent data are at hand for discussion and mature decision. The "group approach" implies the services, when possible, of a radiologist, pathologist, surgeon, internist, and specialist in the given field in which the tumor occurs, i.e., gynecology; orthopedics; eye, ear, nose and throat; urology, etc. Such a "group approach" forms the basis of organization of consultative tumor boards whose establishment is being encouraged in all California hospitals approved by the American College of Surgeons and the Cancer Commission of the California Medical Association. *Hastily selected treatment only too often spells the doom of the cancer patient.*

CANCER RESEARCH

It has been generously estimated that under ideal conditions of early diagnosis and adequate treatment by methods now available, the annual mortality from cancer in the United States could be halved. This would still leave an annual residual of some 100,000 deaths from neoplastic disease. The only means of eradicating this tragic problem is through the experimental approach—research.

Cancer research, or oncology, as an experimental endeavor began only some 50 years ago. The studies of biologists, geneticists, biochemists and scientists in other fields have yielded extensive information, although much of it as yet has had little clinical application. The public and the medical and allied professions have become increasingly aware of the importance of developing this aspect of our attack on cancer. The American Cancer Society and its predecessor, the American Society for the Control of Cancer, with its Woman's Field Army, were leaders in awakening public interest to the necessity of adequate support of scientists working on this engrossing biologic problem of abnormal growth.

The Federal Government, by its Cancer Act of 1937, mobilized the efforts on a nation-wide scale which is being supported by ever-increasing funds. Many large private donations, such as the Donner International Cancer Foundation, the Anna Fuller Fund, the Finney-Howell Foundation, the Jane Coffin Childs Memorial Fund and the recent Sloan-Kettering Foundation, are devoted entirely to the study of cancer. As a result, there are at least six outstanding research institutions in the United States conducting investigations exclusively or chiefly on cancer; perhaps the largest are the National Cancer Institute, Bethesda, Maryland; the Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York; the Barnard Free Skin and Cancer Hospital, St. Louis, and the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine.

Noteworthy programs in cancer research are being conducted in several universities, particularly Yale, Minnesota and Wisconsin. Two magazines, *Cancer Research,* and the *Journal of the National Cancer Institute,* are devoted exclusively to the presentation of results of research work on cancer. The number of separate publications on the subject is well over twenty thousand, and several recent attempts to evaluate and to digest the available information have been made. To readers interested in the field are recommended the following: "Mammary Tumors in Mice," and "A.A.A.S. Research Conference on Cancer," published in 1945 by the American Association for the Advancement of Science, Washington, D. C., the sprightly "Riddle of Cancer" by C. Oberling, published in 1945 by the Yale Press, New Haven, Conn., and the "Biochemistry of Cancer," by J. P. Greenstein, issued in 1947 by the Academic Press, New York.

RESEARCH IN OTHER COUNTRIES

The research efforts against cancer are, of course, not limited to the United States. The Imperial Cancer Research Fund and the Royal Cancer (Free) Hospital of Great Britain have been among the pioneers and remain among the leaders in the field. Laboratories for cancer research in France, the Scandinavain countries and Germany have made some of the outstanding contributions to the subject. The Oncology Institute in Leningrad, as well

PERIODIC PHYSICAL EXAMINATION SHEET

[Cancer Detection]

Name.. Date.................................. Case No.....................

Address.. Telephone No...........

Name and Address of Relative or Friend..

Sex.......................... Age.................... Nationality...

Personal History...

....

Physical Findings................ T................ P................ R................ Wt................ Recent loss?..................

Head and Neck..

Eyes.. Ears.. Nose..

Mouth (incl. Lips, Teeth, Tongue)..

Chest (incl. report of survey film)..

Heart (incl. B.P.)..

Breasts..

Abdomen...

Rectal Exam...

Pelvic Exam...

External Genitalia..

Extremities...

Skin...

Lymph Nodes (neck, axillae, groin, etc.)..

Blood Count................................ Urinalysis................................ Was R..................................

Impression...

Disposition...

Date of Next Examination...

Letter sent to referring or family physician..

Date.. ...., M.D., Examiner

NOTE: Enter significant findings, including laboratory data, on additional sheet as necessary.

Form 1-46

Figure 1.—"Periodic physical examination sheet (cancer detection)" recommended by the Cancer Commission of the California Medical Association for use in the private physician's office.

as other laboratories in Moscow and in Kiev have also made important scientific additions to our knowledge.

Oncology is not a science in itself but the application of many scientific disciplines to the problem of neoplastic diseases. The development of microscopic techniques during the nineteenth century permitted a detailed study of tumors and established the morphologic criteria upon which the taxonomy, differential diagnosis and prognosis of cancer are still based. At the turn of the century, careful studies by the Imperial Cancer Research Fund and others, established that neoplastic diseases were prevalent in a number of species of animals, particularly mice, and that these tumors in all ways were comparable to similar neoplasms in man. It is now known that every species that has been sufficiently studied develops malignant neoplasms. This includes lower forms such as amphibia and fish as well as mammals. Even plants develop cellular overgrowths that resemble cancer.

It was found that certain tumors could be transplanted and grown in new hosts of the same species. The proper material for experimentation, in unlimited amounts, thus became available, and a fertile decade of study of transplanted tumors had its inception. Although much was learned regarding the characteristics of tumor tissue, this material gave no insight into the mechanism of tumor development. It was, in effect, a form of *in vivo* tissue culture. Refinements to tissue culture were also undertaken when proper methods had been developed by Harrison and by Carrel. They are still being actively pursued.

Perhaps the most striking new development in this field are the observations of Earle and of Gey that malignant transformation of normal fibroblasts into sarcoma can occur in cells grown in tissue culture for protracted periods. Thus, at least this type of neoplasm can arise from cells entirely divorced from the systemic reactions of the original host. Interesting data have become available from investigations on the growth of neoplasms in developing chick eggs, and in the anterior chamber of the eye of species other than those in which the tumors arose. Apparently the immunologic reactions that do not permit heterotransplantation under usual conditions are not operative in these media.

During the transplantation decade numerous attempts were made to demonstrate infectious agents of the bacterial type in the etiology of the tumors. All these attempts have been disproven; the transfer of viable cells was apparently required for successful transplantation. Rous, in 1911, showed that certain sarcomas in chickens could be transmitted by material that had been passed through filters that retained cells and bacteria. At this time the concept of filterable viruses as a pathogenic entity was not sufficiently developed, and the work was not generally accepted. Recently the role of viruses in the etiology of certain types of neoplasms in mammals as well as in birds has again come to the fore.

In the second decade of the century, the main emphasis began to be placed upon the study of genetic factors in the development of tumors. Cancer, like every other feature of the living organism, is the product of environment (extrinsic factors) acting upon the inborn constitution of the organism or its tissues (intrinsic factors). It was soon shown that cancer was not inherited as a simple character, although susceptibility to cancer in varying degrees is determined by the genetic pattern. Moreover, this genetic pattern is not the same for all neoplasms. In order to reach this important conclusion, geneticists had to develop strains of mice that were generally "pure" or homozygous. These strains of mice are an invaluable material for cancer work since they display fairly constant incidences of specific types of tumors, and have rightfully been stated to be as essential to biologists as are pure chemicals to chemists.

In 1918, Japanese workers first showed that long-continued applications of tar to the ears of rabbits induced carcinoma. A simple, controllable method of inducing cancer in animals, as well as propagating it, now became available. It was not until 1930 that British scientists isolated from tar the specific chemical, 3,4-benzpyrene, that had the power of inducing malignant neoplasms in animals and, presumably, in man. With the isolation of pure carcinogenic compounds and the synthesis of one of the most powerful of them, 20-methylcholanthrene, from bile acids, it became popular to postulate that cancer may be the result of synthesis by the body of carcinogens related to the polycyclic hydrocarbons, with perhaps cholesterol as the precursor. At the same time, chemists clarified the molecular structure of steroid hormones, and estrogenic compounds were shown to have the power of inducing a number of neoplasms in animals, including those of the breast, uterus, testis and the pituitary gland.

Extension of the work, however, showed that a large number of chemicals of unrelated structure, including certain azo dyes, acetylfluorene, carbon tetrachloride, repeated subcutaneous injections of certain simple acids and sugars, and even bakelite discs also evoked tumors in animals. The list of substances able to evoke tumors in animals under certain specific conditions now extends to over 250 compounds and no characteristic molecular structure as a common explanation can be maintained. It was also shown that two forms of physical energy, roentgen rays and ultraviolet rays, also had the property of eliciting the neoplastic reaction. Roentgen rays, of course, are well known to produce carcinoma in man as well as in animals, and the higher incidence of cutaneous carcinoma in our southern states may well be correlated to the increased exposure to ultraviolet radiations.

STUDY OF SPECIFIC NEOPLASMS

In contrast to the overall scientific attack on cancer as an entity, certain lines of investigation have emphasized the detailed study of specific neoplasms. Relatively few experimental tumors, among them the mammary, pulmonary and hepatic tumors and leukemia in mice, have been sufficiently studied by this approach. Data are sufficient, however, to conclude that, at least during the stage of initiation, cancer should be considered as a great group of diseases of varying etiologies and involving, different determining factors.

Mammary tumors in mice, a biologic entity showing a variety of morphological patterns, usually arise multicentrically from the terminal buds of the gland, grow progressively, metastasize and kill the host, and in other ways exhibit characteristics of typical malignant neoplasms. Strains of mice developing practically 100 per cent mammary tumors among the females, and strains that have practically no mammary tumors have been developed through many generations of careful inbreeding and selection. Breeding females develop more tumors at an earlier age than non-breeding animals, and oophorectomy sharply reduces the incidence. Mammary tumors can be induced in male mice of strains in which the females develop brest tumors by transplantation of ovaries, or by injection of estrogenic compounds. The classical study of the inheritance of these tumors, by the Jackson Memorial Laboratory group, showed that the transmission was extra-chromosomal in nature. The progeny of high-mammary-tumor females crossed to low-tumor males developed mammary tumors regularly; but when the cross was reversed—that is, the female came from the low-tumor strain and the male from the high-tumor strain—practically no mammary tumors developed in the hybrid progeny despite their identical genetic make-up.

Bittner continued these studies by simply transferring upon birth the high-mammary-tumor mice to low-tumor females, and the young did not develop mammary tumors. Conversely, mice of low-tumor strains that were foster nursed by high-tumor females developed many breast tumors. Active investigations have now established that there is an agent in the milk, as well as in many tissues of the high-tumor lines, which is self-reproducing, filterable, and by ultraviolet spectrography and ultracentrifugation tests falls in the general category of viruses.

Mammary tumors in mice appear to be the result of an intricate interplay between at least three sets of factors: the genetic, the hormonal, and the milk agent; in addition, the appearance of these neoplasms is sharply influenced by environmental factors such as diet, and by injection of carcinogenic compounds such as methylcholanthrene. The neoplasm can be added to a number of other tumors in which a filterable virus entity is implicated etiologically; the Rous sarcoma of chickens, and the Shope papilloma and carcinoma of rabbits. Whether these viruses are more than the initiators of the neoplastic transformation, that is, whether cancer is a form of virus-cell symbiosis, however, remains a matter of conjecture.

The specificity of the etiologic factors involved in the genesis of different neoplasm is well illustrated in the mouse, in which the milk agent appears to be involved only in the genesis of mammary tumors. Hepatomas and pulmonary tumors do not require the presence of the agent. Hormones do not influence the genesis of pulmonary tumors, and they play a minor role in hepatic tumors. Certain azo dyes, such as o-aminoazotoluene, induce hepatomas, increase slightly the incidence of pulmonary tumors and have no effect on mammary carcinogenesis; ethyl carbamate (urethane) markedly increases the incidence of pulmonary tumors but so far has not been described to be involved in the genesis of other tumors in the mouse. Certain restrictions in the diet retard the development of mammary tumors but accelerate the appearance of hepatic tumors in mice receiving the azo dyes, and have no effect on the genesis of pulmonary tumors.

RESEARCH BY BIOCHEMISTS

About 20 years ago biochemists actively joined the ranks of cancer research workers. They have made noteworthy investigations in the problem, particularly in the study of the biochemical characteristics of neoplastic tissue. By far the greatest single contribution has been that of Warburg, who showed that malignant tumors may be characterized by their metabolism, by the consideration of the absolute and relative magnitudes of anaerobic glycolysis, of the respiratory quotient and of aerobic glycolysis. The metabolism of tumors and other living tissues is governed by diverse and intricate systems of enzymes. A methodical investigation of many of the known enzyme systems has been made of many tumors and the results have been compared with values obtained with normal tissues of origin. No enzyme or chemical specific for neoplasm has been uncovered. In general, tumors show less variety in their content of enzymes or of vitamins than do normal tissues, thus tending to converge toward a common class which in some respects resembles embyronic tissue. It may be stated that the enzyme and vitamin content of neoplastic tissues is usually at the lower end of normal values, indicating that neoplasms have a low reserve—perhaps because most of their energy is expended toward reproduction and growth rather than toward activities useful to the organism.

The biochemical studies have also indicated that profound alterations occur in the organism bearing a neoplasm, at sites far distant from the tumor. Catalase activity in the liver and kidneys is reduced; perhaps this effect is associated with decreased hematin synthesis. Hemoglobin is also reduced in the presence of a neoplasm. There are alterations in the adrenal cortex, which may be associated with cachexia of cancer, and the group at Memorial Hospital is pursuing the problem of altered steroid compounds related to the adrenocortical hormones that appear in the urine of patients with cancer. Hepatic function is impaired in patients with gastric or intestinal neoplasms, and these functions are partially restored upon the removal of the tumors. The biochemical effects of certain specific types of neoplasm already have gained recognition as laboratory tests of great clinical value. Among these may be mentioned the alterations in alkaline phosphatase in neoplasms of bone and liver, in acid phosphatase in the presence of prostatic carcinoma, the Bence-Jones proteins in myeloma, melanin in the urine of patients with melanoma, and various endocrine effects of tumors of the pancreas, adrenal, thyroid, pituitary, ovary and testis.

The modern trends in cancer research can be outlined under three general headings. The first approach that is going to receive emphasis is that of *cellular physiology*—the attack on the structure, function and reactions not only of the cell, the unit of living matter, but of its components as well. Methods of histochemistry, refined techniques of determining electrical potential and other physical characteristics, and the use of tracer elements to assist in the unraveling of the complex structure of nucleoproteins will be mobilized and exploited. The second approach is the closely related *study of the intermediate mechanisms involved in the transformation of normal into neoplastic tissue.* So far, studies have been limited to the two ends of the reaction: the normal has been compared with the frankly neoplastic, with the great intermediary stages remaining *terra incognita.* Emphasis will be placed upon the study of the development of neoplastic transformation through all its stages. Steps in this direction are already developing in the work of Cowdry and his group in St. Louis.

In contrast with the fundamental approaches indicated above, the third line of attack that is being actively pursued are the semi-empirical all-out programs of *experimental chemotherapy* of neoplasms at the National Cancer Institute, at the Memorial Hospital, and in Englannd. This involves the systematic synthesis and assay of compounds exhibiting effects on experimental tumors, elaboration and alteration of the chemical structure in hopes of attaining more selective and more pronounced action. Even at this early stage of developments, nitrogen mustards, the polysaccharide derived from Bacillus prodigiosus, and stilbamidine have been shown to have some action on certain neoplasms in man.

Every year scientific advances have enhanced our knowledge and made it possible to save more people from cancer. Large gaps remain, and many findings seem to be contradictory. Cancer research must proceed firmly along two lines: the study of carcinogenesis, which will give us an insight into the prophylaxis and prevention of cancer, and the study of characteristics of tumor growth, which will give us the clue to its control. At this stage of research, all-inclusive theories of cancer, not matter how glittering they may seem in an armchair, are more of a hindrance than a help in the careful, analytical approaches that must be pursued and individualized for each type of neoplastic growth until we have sufficient information to synthesize our data into a coherent whole. We are at present not as far along with our research in the ultimate solution and reversability of cancer as were the physicists in 1941 with atomic energy.

The atom bomb project was a gigantic application of knowledge that had been previously discovered. In cancer research we do not have as yet a comparable amount of fundamental information. We must soberly recognize this fact and guard against the disappointments of expecting too much too soon. Generous, continual financial support, an accentuated group effort in which many scientific fields are strongly represented and in which the competent cancer investigators have an adequately compensated and assured status are prerequisites for continued and accelerated progress. The most important elements, however, are conscientious scientific effort and patience, slow and exasperating though the work occasionally may seem. With confidence in the experimental method and the philosophy of science, and with tools of ever-increasing power and subtlety, it is certain that the efforts will ultimately yield the key to and the mastery over neoplastic growth.

Chapter II—"General Principles in the Treatment of Cancer," by Emile Holman, M.D., and Chapter III "The Examination of the Cancer Patient," by Otto Pflueger, M.D., will appear in this section next month.

BIBLIOGRAPHY

Minimum Standards for Cancer Detection Centers in California, Cancer Commission, California Medical Association, Revised (Jan. 18), 1947.

Minimum Standards for Consultative Tumor Boards, Cancer Commission, California Medical Association, Revised (Jan. 18), 1947.